Claims

1. A nucleotide sequence coding for a protein present in invertebrate and/or vertebrate organisms, said nucleotide sequence coding for a protein comprising a positive function in a regulatory pathway.

2. The nucleotide sequence according to claim 1, wherein said pathway is the Wnt/Wg-pathway.

3. The nucleotide sequence according to claims 1 and 2, wherein the function of the encoded protein comprises the function of legless (lgs) gene products.

4. The nucleotide sequence according to claims 1-3, wherein said nucleotide sequence is coding for Drosophila Legless (Lgs) protein.

5. The nucleotide sequence according to claim 4, wherein said nucleotide sequence comprises the sequence as shown in Figure 2.

6. The nucleotide sequence according to claims 1-3, wherein said nucleotide sequence is coding for human Legless (hLgs) proteins.

7. The nucleotide sequence according to claim 6, wherein said nucleotide sequence include the sequence as shown in Figure 10.

8. A nucleotide sequence comprising at least 50% homology to (a) the nucleotide sequence or stretches of the nucleotide sequence as shown in Figures 2 and 10 or (b) complements or fragments thereof.

9. The nucleotide sequence according to any of claims 1 to 8, wherein fragments of said sequence are used as probes in hybridization assays.

10. A vector comprising the nucleic acid according to any of claims 1 to 8.

11. The vector of claim 10 operably linked to control sequences recognized by a host cell transformed with said vector.

12. A host cell containing the vector of claims 10 and 11 selected from the group consisting of mammalian, bacterial, yeast, plant and insect cells.

13. A polypeptide derived from any of the nucleotide sequences of claims 1 to 8, derivatives, fragments and analogs thereof.

14. The polypeptide of claim 13, comprising the function of Legless proteins.

15. A polypeptide sharing one or more homologue amino acid domains with the Legless protein being a functional homologue of legless.

16. The polypeptide according to claim 15, wherein said functional homologue is the hLgs/Bcl-9 protein or a fragment thereof, comprising the function of Legless protein in the Wnt-pathway.

17. Use of the polypeptide according to any of claims 13-16 for the isolation of Lgs-binding proteins by carrying out a co-immunoprecipitation assay.

18. A process for producing a polypeptide according to claim 13 to 16 comprising culturing the host cell of claim 12 under conditions suitable for expression of said polypeptide and

recovering said protein or fragment thereof from the cell culture.

19. An antibody which specifically binds to the polypeptides of claims 13 to 16, selected from the group consisting of polyclonal antibodies, monoclonal antibodies, humanized antibodies and single chain antibodies.

20. A chimeric molecule comprising the polypeptide of any of claims 13-16 or a fragment thereof fused to a heterologous amino acid sequence.

21. The chimeric molecule according to claim 20, wherein said heterologous amino acid sequence is selected from the group comprising an epitope tag sequence, a glutathione-S-transferase moiety, a thioredoxin moiety, and an antibody moiety.

22. Use of the polypeptide according to claim 20-21 for the isolation of Lgs-binding proteins by carrying out an assay selected from the group consisting of an in vitro-binding assay with such a peptide, or a co-immunoprecipitation from vertebrate or invertebrate cell lysates or a mammalian or yeast two hybrid assay.

23. A peptide, comprising a stretch of amino acids comprising at least one sequence homology domain, which is common between the Drosophila Legless and human Legless proteins.

24. The peptide according to claim 23, wherein the common domains from human Legless are derived from hLgs-1 or hLgs/Bcl9.

25. Compound interfering with the binding to the domains according to claims 23-24 for inhibiting the interaction between partner proteins to these domains by exposing said domains to said compounds.

26. The compound according to claim 25, wherein said partner proteins are Dll1 and β-Catenin.

27. The compound according to claims 25 and 26, wherein said compounds are selected from a group consisting of small peptides, synthetic polymers, and natural or synthetic chemical compounds.

28. The compound according to claims 25 and 26, wherein said compound is a small peptide comprising the sequence homology domain 1 or 2 of figure 7.

29. Use of the compound according to claim 28 in a pharmaceutical composition delivering said peptide or its relative nucleic acid sequence in an appropriate vector into a cancerous cell.

30. A synthetic molecule, simulating the function of Legless proteins in the Wnt pathway.

31. An antagonist of the polypeptide of claims 13-16 selected from the group comprising small bioorganic molecules, synthetic polymers, or small polypeptides.

32. An agonist of the polypeptide according to claims 13-16, selected from the group comprising small polypeptides, and small bioorganic molecules.

33. A method of screening for agonists and/or antagonists of the polypeptide claimed in claims 13-16 for functional activity.

34. The method according to claim 33, wherein said method is a HTRF based protein-protein-interaction assay.

35. An antisense oligonucleotide sequence derived from the nucleotide sequences according to claims 1 to 8.

36. The antisense oligonucleotide sequence according to claim 35, wherein said oligonucleotide sequence hybridizes to RNA and/or genomic DNA encoding a vertebrate Lgs.

37. The antisense oligonucleotide sequence according to claims 35 and 36, wherein said oligonucleotide sequence prevents translation of said RNA or transcription of said DNA.

38. The antisense oligonucleotide sequence according to claims 35 to 37, wherein said oligonucleotide sequence comprises chemically modified nucleotides or nucleotide analogs.

39. Use of the antisense oligonucleotides according to claims 35-38 in the therapy of diseases caused by an over-activation of the Wg pathway.

40. A double-stranded RNA sequence derived from the nucleotide sequences according to claims 1 to 8 comprising RNA interfering activities.

41. The double-stranded RNA sequence according to claim 40, wherein said double-stranded RNA sequence is able to induce degradation of lgs single stranded RNA.

42. Use of the double-stranded RNA according to claims 40 and 41 for reducing lgs gene expression in an invertebrate or vertebrate organism or an invertebrate or vertebrate cell line.

43. A pharmaceutical composition comprising an oligonucleotide derived from the nucleotide sequence according to any of claims 1-8, further comprising an acceptable pharmaceutical carrier, said oligonucleotide and said pharmaceutical carrier being capable of passing through a cell membrane.

44. A pharmaceutical composition derived from the polypeptide of claim 16 further comprising an acceptable pharmaceutical carrier, said pharamceutical composition being an oligonucleotide and said

pharmaceutical carrier are capable of passing through a cell membrane.

45. The pharmaceutical composition according to claims 43 and 44, wherein said oligonucleotide is capable of reducing the expression of a mammalian Lgs protein.

46. The pharmaceutical composition according to claims 43 to 45, wherein said oligonucleotide is coupled to a moiety that inactivates mRNA.

47. The pharmaceutical composition according to claim 46, wherein the moiety inactivating mRNA is a ribozyme (ribozyme is an enzyme).

48. The pharmaceutical composition according to claims 43 to 47, wherein the pharmaceutically acceptable carrier comprises a structure binding to a receptor on a cell surface, said structure being taken up by the cell after binding to said receptor.

49. The pharmaceutical composition according to claims 43 to 46, wherein said oligonucleotide is the double stranded RNA molecule of claims 37 and 38.

50. The pharmaceutical composition according to claim 49, wherein the double stranded RNA molecule comprises 18 to 1000 nucleotides, preferably 20 to 500 nucleotides, more preferably 20 to 50 nucleotides and most preferably 20 to 22 nucleotides.

51. A therapeutic method comprising the use of Lgs proteins, homologues thereof, functional homologues, nucleic acids and/or fragments thereof for the treatment of disorders of cell fate, comprising the administration of a therapeutic compound.

52. The therapeutic method according to claim 51, said disorders of cell fate being differentiation or proliferation.

53. The therapeutic method according to claim 51, comprising the administration of a therapeutic compound selected from the group consisting of invertebrate and vertebrate Lgs protein homologues or fragments thereof, antibodies, antibody fragments, Lgs antisense DNA, *lgs* antisense RNA, *lgs* double-stranded RNA, small peptides, chemical and natural compounds being capable of interfering with Lgs function, synthesis and degradation.

54. The therapeutic method according to claims 51-53, wherein the therapeutic compound is administered to treat a cancerous condition.

55. The therapeutic method according to claims 51-53, wherein the therapeutic compound is administered to prevent progression from a pre-neoplastic or non-malignant condition to a neoplastic or malignant state.

56. The therapeutic method according to claims 51-53, wherein the therapeutic compound is administered to treat a cancerous condition characterized by over-stimulation of the Wnt pathway.

57. The therapeutic method according to claims 51-53, wherein the cancerous condition is colon, breast, head and neck, brain, tyroid, medulloblastoma or skin cancer.

58. The therapeutic method according to claims 51-53, wherein the therapeutic compound is administered to a blood disease.

59. The therapeutic method according to claims 51-53, wherein the therapeutic compound is administered to promote tissue regeneration and repair.

60. A method for diagnosing disorders of cell fate comprising the use of anti-Lgs antibodies, Lgs proteins or homologues thereof, lgs nucleic acids and/or fragments thereof.